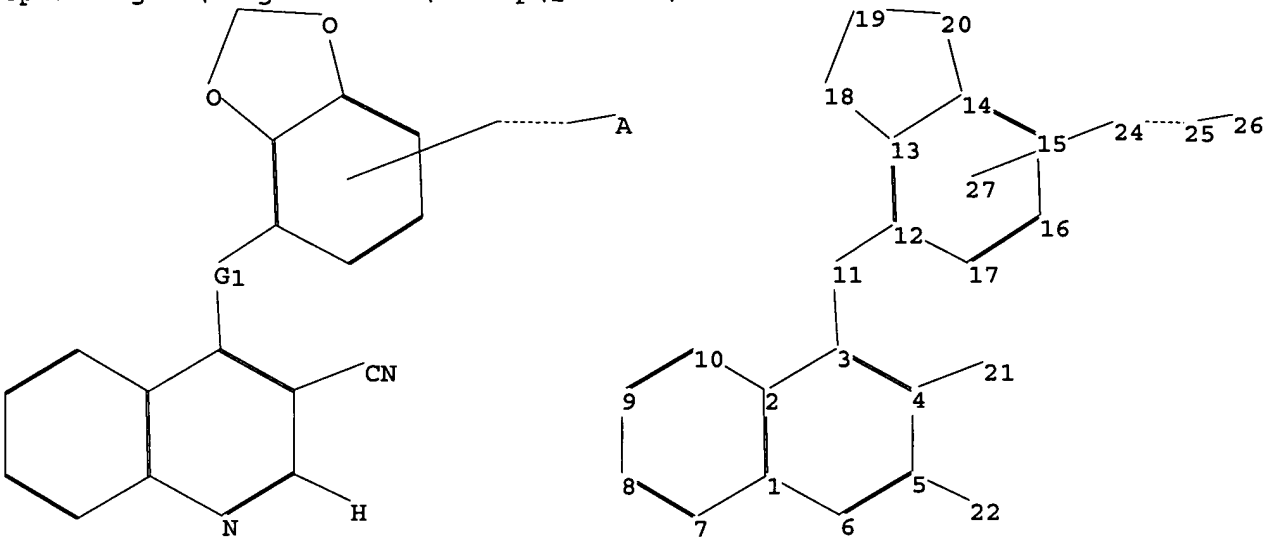
10/520,468

* * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:11:39 ON 08 MAR 2006

=> file reg

=>
Uploading C:\Program Files\Stnexp\Queries\10532958.str



chain nodes :
11 21 22 24 25 26
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17 18 19 20
chain bonds :
3-11 4-21 5-22 11-12 24-25 25-26
ring bonds :
1-2 1-6 1-7 2-3 2-10 3-4 4-5 5-6 7-8 8-9 9-10 12-13 12-17 13-14 13-18
14-15 14-20 15-16 16-17 18-19 19-20
exact/norm bonds :
3-11 11-12 24-25 25-26
exact bonds :
4-21 5-22 13-18 14-20 18-19 19-20
normalized bonds :
1-2 1-6 1-7 2-3 2-10 3-4 4-5 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
isolated ring systems :
containing 1 : 12 :

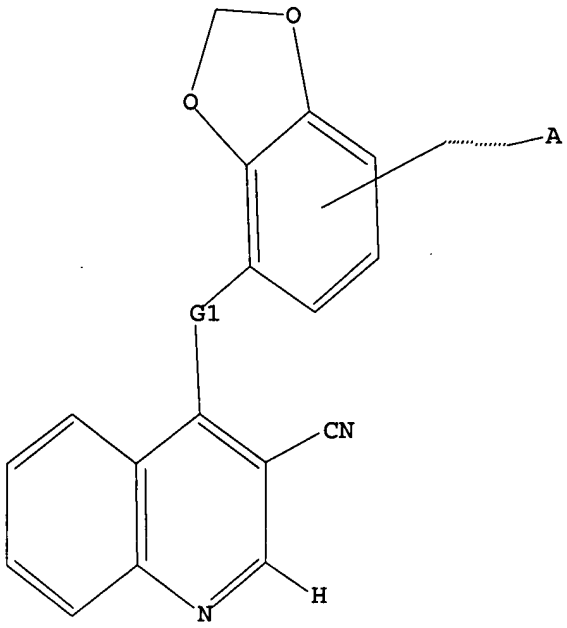
G1:C,O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:CLASS 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L1 STRUCTURE UPLOADED

page

```
=> d l1
L1 HAS NO ANSWERS
L1                STR
```




```
G1 C,O,S,N
```

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 full
L3            69 SEA SSS FUL L1

=> file ca


=> s l3
L4             3 L3

=> d ibib abs fhitstr hitrn 1-3
```

L4 ANSWER 1 OF 3 CA COPYRIGHT 2006 ACS on STN

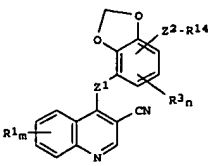
ACCESSION NUMBER: 140:93942 CA
TITLE: Preparation of substituted 3-cyanoquinolines with MAP kinase inhibitory activity as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Gibson, Keith Hopkinson; Foote, Kevin Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005284	A1	20040115	WO 2003-GB2882	20030704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003281351	A1	20040123	AU 2003-281351	20030704
EP 1521751	A1	20050413	EP 2003-740770	20030704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501185	T2	20060112	JP 2004-518961	20030704

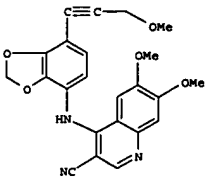
PRIORITY APPLN. INFO.: GB 2002-15823 A 20020709
WO 2003-GB2882 W 20030704

OTHER SOURCE(S): MARPAT 140:93942
GI

L4 ANSWER 1 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)



I



II

AB The invention concerns substituted 3-cyanoquinolines (shown as I; variables defined below; e.g. II), processes for their preparation, pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an anti-invasive or anti-proliferative agent (no data) in the containment and/or treatment of solid tumor disease. Compds. I possess p44MAP kinase inhibitory activity (no data). For I: Z1 is an O, S, SO, SO2, N(R2) or C(R2)2 (R2 = H or (1-6C)alkyl); m is 0-4; each R1 group = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, etc. N = 0-3; each R3 = halo, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, etc.; Z2 is C.tplbond.C or C(R13):C(R13) (R13 = H or (1-6C)alkyl); and R14 = halo, cyano, isocyano, formyl, carboxy, carbamoyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxycarbonyl, etc.; addnl. details are given in the claims. Methods of preparation are claimed and 24 example preprns. are included. For example, II was prepared from 3-cyano-4-(4-iodo-2,3-methylenedioxyanilino)-6,7-dimethoxyquinoline, Me 2-propynyl ether, tetrakis(triphenylphosphine)palladium(0), cuprous iodide and Et2NH; preprns. of the reactants are described.

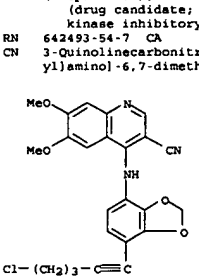
IT **642493-54-7P**, 4-[4-(5-Chloro-1-pentynyl)-2,3-

L4 ANSWER 1 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)

methylenedioxyanilino]-3-cyano-6,7-dimethoxyquinoline
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of substituted 3-cyanoquinolines with MAP kinase inhibitory activity as antitumor agents)

RN 642493-54-7 CA

CN 3-Quinolinecarbonitrile, 4-[[7-(5-chloro-1-pentynyl)-1,3-benzodioxol-4-yl]amino]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



IT **642493-54-7P**, 4-[4-(5-Chloro-1-pentynyl)-2,3-methylenedioxyanilino]-3-cyano-6,7-dimethoxyquinoline **642493-64-9P** **642493-65-0P** **642493-77-4P**, trans-3-Cyano-6,7-dimethoxy-4-[[7-[2-(methoxycarbonyl)vinyl]benzodioxol-4-yl]amino]quinoline **642493-80-9P**, (2E)-3-[4-[(3-Cyano-6,7-dimethoxyquinolin-4-yl)amino]-2,3-(methylenedioxy)phenyl]acrylic acid **642493-92-3P**,

3-Cyano-4-[6-chloro-4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]quinoline
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of substituted 3-cyanoquinolines with MAP kinase inhibitory activity as antitumor agents)

IT **642493-47-8P**, 3-Cyano-6,7-dimethoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline monohydrochloride **642493-48-9P**, 3-Cyano-6,7-dimethoxy-4-[6-chloro-4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-49-0P**, 3-Cyano-7-ethoxy-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline monohydrochloride **642493-51-4P**,

3-Cyano-6,7-dimethoxy-4-[4-[3-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)-1-propynyl]-2,3-methylenedioxyanilino]quinoline **642493-52-5P**, 3-Cyano-6,7-dimethoxy-4-[2,3-methylenedioxy-4-[3-(morpholino)-1-propynyl]anilino]quinoline dihydrochloride **642493-53-6P**, 3-Cyano-6,7-dimethoxy-4-[2,3-methylenedioxy-4-[3-(piperazin-1-yl)-1-propynyl]anilino]quinoline dihydrochloride **642493-55-8P**, 3-Cyano-6,7-dimethoxy-4-[2,3-methylenedioxy-4-[5-(morpholino)-1-pentynyl]anilino]quinoline dihydrochloride **642493-56-9P**,

3-Cyano-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline trihydrochloride **642493-57-0P**, 3-Cyano-6-methoxy-7-(3-morpholinopropoxy)-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline dihydrochloride

L4 ANSWER 1 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)

642493-58-1P, 3-Cyano-6-methoxy-7-[3-(morpholino)propoxy]-4-[[5-chloro-7-(3-methoxyprop-1-ynyl)benzodioxol-4-yl]amino]quinoline dihydrochloride **642493-59-2P**, 3-Cyano-6-methoxy-7-[3-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)propoxy]-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline dihydrochloride **642493-60-5P**, 3-Cyano-6-methoxy-7-(2-fluoroethoxy)-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline monohydrochloride **642493-61-6P**, 3-Cyano-6-methoxy-7-[3-(3-oxopiperazin-1-yl)propoxy]-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline **642493-62-7P**, 3-Cyano-6-methoxy-7-[3-(3-oxopiperazin-1-yl)propoxy]-4-[[5-chloro-7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline dihydrochloride **642493-63-8P**, 3-Cyano-6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[[7-(3-methoxy-1-propynyl)benzodioxol-4-yl]amino]quinoline monohydrochloride **642493-71-8P**, 3-Cyano-7-[3-[4-(2-fluoroethyl)piperazin-1-yl]propoxy]-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline dihydrochloride **642493-73-0P**, 7-[3-(4-Acetylpiperazin-1-yl)propoxy]-3-cyano-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline dihydrochloride **642493-74-1P**, 3-Cyano-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]-7-[2-[2-(pyrrolidin-1-yl)ethoxy]ethoxy]quinoline dihydrochloride **642493-75-2P**, trans-3-[4-[(3-Cyano-6,7-dimethoxyquinolin-4-yl)amino]-2,3-(methylenedioxy)phenyl]acrylonitrile **642493-76-3P**, trans-3-Cyano-6,7-dimethoxy-4-[[5-chloro-7-(2-cyanovinyl)benzodioxol-4-yl]amino]quinoline **642493-78-5P**, trans-3-Cyano-6,7-dimethoxy-4-[[5-chloro-7-[2-(methoxycarbonyl)vinyl]benzodioxol-4-yl]amino]quinoline **642493-79-6P**, trans-3-Cyano-6,7-dimethoxy-4-[[7-(2-propionylvinyl)benzodioxol-4-yl]amino]quinoline **642493-81-0P**, N-[(2E)-3-[4-[(3-Cyano-6,7-dimethoxyquinolin-4-yl)amino]-2,3-(methylenedioxy)phenyl]acryloyl]morpholine **642493-82-1P**, (2E)-3-[4-[(3-Cyano-6,7-dimethoxyquinolin-4-yl)amino]-2,3-(methylenedioxy)phenyl]-N-(2-methoxyethyl)acrylamide **642493-83-2P**, (2E)-3-[4-[(3-Cyano-6,7-dimethoxyquinolin-4-yl)amino]-2,3-(methylenedioxy)phenyl]-N-(2-methoxyethyl)-N-methylacrylamide **642493-84-3P**, 3-Cyano-6,7-dimethoxy-4-[5-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-85-4P**, 3-Cyano-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline dihydrochloride **642493-86-5P**, 3-Cyano-7-[3-(morpholin-4-yl)propoxy]-5-[(tetrahydro-2H-pyran-4-yl)oxy]-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline dihydrochloride **642493-87-6P**,

3-Cyano-7-methoxy-4-[4-(4-methoxy-1-butynyl)-2,3-methylenedioxyanilino]-5-[(1-methylpiperidin-4-yl)oxy]quinoline dihydrochloride **642493-89-8P**, 4-[(4-But-3-en-1-ynyl-2,3-methylenedioxy)anilino]-3-cyano-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]quinoline dihydrochloride **642493-90-1P**, 4-[4-(1-Chloro-4-methyloxybut-1-enyl)-2,3-methylenedioxyanilino]-3-cyano-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]quinoline dihydrochloride **642493-91-2P**,

3-Cyano-4-[6-chloro-4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]quinoline dihydrochloride **642493-94-5P**, 7-[3-(4-Acetylpiperazin-1-yl)propoxy]-3-cyano-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-95-6P**, 3-Cyano-6,7-dimethoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-96-7P**, 3-Cyano-7-ethoxy-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-97-8P**, 3-Cyano-7-[3-[4-(2-fluoroethyl)piperazin-1-yl]propoxy]-6-methoxy-4-[4-(3-

L4 ANSWER 1 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)
methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline **642493-98-9P**, 3-Cyano-6-methoxy-7-[3-(4-methylpiperazin-1-

yl)propoxy]-4-[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinolin
e **642493-99-0P**, 3-Cyano-6-methoxy-4-[4-(3-methoxy-1-propynyl)-
2,3-methylenedioxyanilino]-7-[3-(morpholino)propoxy]quinoline
642494-00-6P, 4-[6-Chloro-4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]-3-cyano-6-methoxy-7-[3-
(morpholino)propoxy]quinoline **642494-01-7P**, 3-Cyano-7-[3-(1,1-
dioxotetrahydro-4H-1,4-thiazin-4-yl)propoxy]-6-methoxy-4-[4-(3-methoxy-1-
propynyl)-2,3-methylenedioxyanilino]quinoline **642494-02-8P**,
3-Cyano-7-(2-fluoroethoxy)-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]quinoline **642494-03-9P**,
3-Cyano-6-methoxy-4-[6-chloro-4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]-7-[3-(3-oxopiperazin-1-yl)propoxy]quinoline
642494-04-0P, 3-Cyano-6-methoxy-4-[4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]-7-[2-[2-(pyrrolidin-1-yl)ethoxy]ethoxy]quinoline
642494-05-1P, 3-Cyano-6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[4-
(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline
642494-06-2P, 3-Cyano-7-methoxy-5-[(1-methylpiperidin-4-yl)oxy]-4-
[4-(3-methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline
642494-07-3P, 3-Cyano-7-[3-(morpholin-4-yl)propoxy]-5-[(tetrahydro-
2H-pyran-4-yl)oxy]-4-[4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]quinoline **642494-08-4P**,

3-Cyano-7-methoxy-4-[4-(4-methoxy-1-butynyl)-2,3-methylenedioxyanilino]-5-
[(1-methylpiperidin-4-yl)oxy]quinoline **642494-09-5P**,

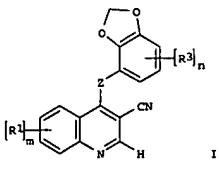
4-[(4-But-3-en-1-ynyl-2,3-methylenedioxy)anilino]-3-cyano-7-methoxy-5-[(1-
methylpiperidin-4-yl)oxy]quinoline **642494-10-8P**,
3-Cyano-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]-4-[6-fluoro-4-(3-
methoxy-1-propynyl)-2,3-methylenedioxyanilino]quinoline
642494-11-9P, 3-Cyano-6-methoxy-7-[2-fluoro-3-(4-hydroxypiperidin-
1-yl)propoxy]-4-[4-(3-methoxy-1-propynyl)-2,3-
methylenedioxyanilino]quinoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(drug candidate; prepn. of substituted 3-cyanoquinolines with MAP
kinase inhibitory activity as antitumor agents)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 2 OF 3 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:36516 CA
TITLE: Preparation of benzodioxolyl substituted quinolines as
antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Gibson, Keith Hopkinson; Poote, Kevin Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

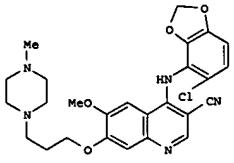
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047582	A1	20030612	WO 2002-GB5496	20021205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002365664	A1	20030617	AU 2002-365664	20021205
PRIORITY APPLN. INFO.:			EP 2001-403128	A 20011205
			WO 2002-GB5496	W 20021205

OTHER SOURCE(S): MARPAT 139:36516
GI

L4 ANSWER 2 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)



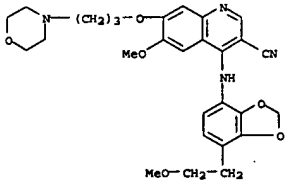
I



II

AB The title compds. [I; Z = O, S, SO, SO2, etc.; m = 0-4; R1 = halo, CF3, CN, etc.; n = 0-3; R3 = halo, CF3, CN, etc.], useful as an anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of the quinoline II was given. The compds. I tested had IC50's < 0.5 μM in assay to detect MEK inhibition.
IT **492443-62-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodioxolyl substituted quinolines as antitumor agents)
RN 492443-62-6 CA
CN 3-Quinolinecarbonitrile, 6-methoxy-4-[[7-(2-methoxyethyl)-1,3-benzodioxol-4-yl]amino]-7-[3-(4-morpholinyl)propoxy]-, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)



●2 HCl

IT **492443-62-6P 492443-96-6P 492444-00-5P**
492444-01-6P 543730-62-7P, 4-[4-(2-Methoxyethyl)-2,3-methylenedioxyanilino]-3-cyano-6-methoxy-7-(3-morpholinopropoxy)quinoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodioxolyl substituted quinolines as antitumor agents)
IT **492443-72-8P**, 7-(3-Chloropropoxy)-3-cyano-6-methoxy-4-[4-(2-methoxyethyl)-2,3-methylenedioxyanilino]quinoline **492444-68-5P**, 3-Cyano-6,7-dimethoxy-4-(2,3-methylenedioxy-4-trimethylsilylethynylanilino)quinoline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzodioxolyl substituted quinolines as antitumor agents)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 3 OF 3 CA COPYRIGHT 2006 ACS on STN

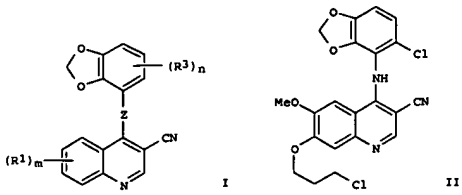
ACCESSION NUMBER: 138:137293 CA
TITLE: Preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors
INVENTOR(S): Hennequin, Laurent Francois Andre
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008409	A1	20030130	WO 2002-GB3177	20020710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1409481	A1	20040421	EP 2002-745602	20020710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2004536860	T2	20041209	JP 2003-513968	20020710
US 2005009867	A1	20050113	US 2004-483782	20040811

PRIORITY APPLN. INFO.: EP 2001-401895 A 20010716
EP 2001-403123 A 20011205
WO 2002-GB3177 W 20020710

OTHER SOURCE(S): MARPAT 138:137293
GI

L4 ANSWER 3 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)



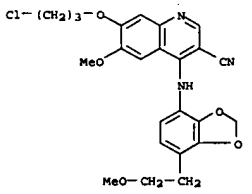
I II

AB Title compds. I [wherein Z = O, S, SO, SO2, NR2, or C(R2)2; R2 = independently H or alkyl; m = 0-4; R1 = independently halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, carbamoyl, alkyl, alkenyl, alkynyl, sulfamoyl, etc.; n = 0-3; R3 = halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, carbamoyl, alkyl, alkenyl, alkynyl, sulfamoyl, etc.; and pharmaceutically acceptable salts thereof] were prepared for use anti-invasive agents in the containment and/or treatment of solid tumor disease. For example, 6-chloro-2,3-methylenedioxyaniline was coupled with 4-chloro-7-(3-chloropropoxy)-3-cyano-6-methoxyquinoline (preparation of starting materials given) to give II. Test compds. inhibited the phosphorylation of a tyrosine containing polypeptide substrate by c-Src kinase and the proliferation of c-Src transfected mouse NIH 3T3 fibroblast cells with IC50 values in the range of 0.001 μM to 10 μM and 0.01 μM to 20 μM, resp. In addition, I inhibited the migration of human A549 tumor cells and the growth of A549 xenograft tumors in athymic nude mice with activities in the range of 0.1 μM to 25 μM and 1-200 mg/kg/day, resp.

IT **492443-72-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor agent; preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors)

RN 492443-72-8 CA
CN 3-Quinolinecarbonitrile, 7-(3-chloropropoxy)-6-methoxy-4-[[7-(2-methoxyethyl)-1,3-benzodioxol-4-yl]amino]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 3 CA COPYRIGHT 2006 ACS on STN (Continued)



IT **492443-72-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor agent; preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors)

IT **492443-62-6P 492443-96-6P 492444-00-5P 492444-01-6P 492444-74-3P**, 3-Cyano-4-[4-(2-cyanoethyl)-2,3-methylenedioxyanilino]-6,7-dimethoxyquinoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors)

IT **492444-68-5P**, 3-Cyano-6,7-dimethoxy-4-(2,3-methylenedioxy-4-trimethylsilylethynylanilino)quinoline **492444-75-4P**, 3-[4-(3-Cyano-6,7-dimethoxyquinolin-4-ylamino)-2,3-methylenedioxyphenyl]acrylonitrile
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/520,468

=> file marpat

=> s l1 full
FULL SEARCH INITIATED 14:12:45 FILE 'MARPAT'
FULL SCREEN SEARCH COMPLETED - 2237 TO ITERATE

100.0% PROCESSED 2237 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.03

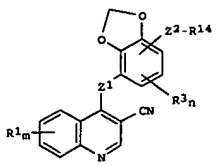
L5 3 SEA SSS FUL L1

=> d ibib abs fqhit 1-3

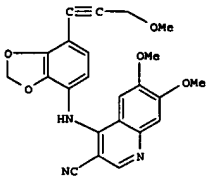
L5 ANSWER 1 OF 3 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:93942 MARPAT
TITLE: Preparation of substituted 3-cyanoquinolines with MAP kinase inhibitory activity as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Gibson, Keith Hopkinson; Foote, Kevin Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005284	A1	20040115	WO 2003-GB2882	20030704
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003281351	A1	20040123	AU 2003-281351	20030704
EP 1521751	A1	20050413	EP 2003-740770	20030704
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006501185	T2	20060112	JP 2004-518961	20030704
PRIORITY APPLN. INFO.:			GB 2002-15823	20020709
			WO 2003-GB2882	20030704

GI



I



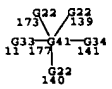
II

AB The invention concerns substituted 3-cyanoquinolines (shown as I; variables defined below; e.g. II), processes for their preparation, pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an anti-invasive or anti-proliferative agent (no data) in the containment and/or treatment of solid tumor disease. Compds. I possess p44MAP kinase inhibitory activity (no data). For I: Z1 is an O, S, SO, SO2, N(R2) or C(R2)2 (R2 = H or (1-6C)alkyl); m is 0-4; each R1 group = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, etc. N = 0-3; each R3 = halo, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, etc.; Z2 is C.tplbond.C or C(R13):C(R13) (R13 = H or (1-6C)alkyl); and R14 = halo, cyano, isocyano, formyl, carboxy, carbamoyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxycarbonyl, etc.; addnl. details are given in the claims. Methods of preparation are claimed and 24 example preprns. are included. For example, II was prepared from 3-cyano-4-(4-iodo-2,3-methylenedioxyanilino)-6,7-dimethoxyquinoline, Me 2-propynyl ether, tetrakis(triphenylphosphine)palladium(0), cuprous iodide and Et2NH; prepns. of the reactants are described.

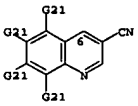
L5 ANSWER 1 OF 3 MARPAT COPYRIGHT 2006 ACS on STN (Continued)
MSTR 1

G4—G1

G1 = 11



G4 = 6



G22 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G25)
G33 = 23

G41 = 20-11 17-141 18-140 19-173 14-139

Patent location: claim 1
Note: or pharmaceutically acceptable salts or protected derivatives
Note: additional derivatization also claimed
Note: substitution is restricted
Note: also incorporates claim 10

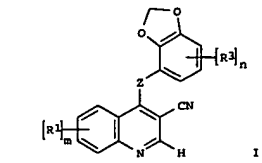
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 2 OF 3 MARPAT COPYRIGHT 2006 ACS on STN

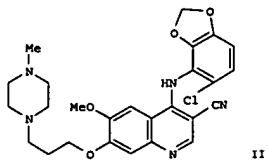
ACCESSION NUMBER: 139:36516 MARPAT
TITLE: Preparation of benzodioxolyl substituted quinolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Gibson, Keith Hopkinson; Foote, Kevin Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047582	A1	20030612	WO 2002-GB5496	20021205
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002365664	A1	20030617	AU 2002-365664	20021205
PRIORITY APPLN. INFO.:			EP 2001-403128	20011205
			WO 2002-GB5496	20021205

GI



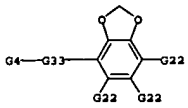
I



II

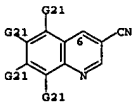
AB The title compds. [I; Z = O, S, SO, SO2, etc.; m = 0-4; R1 = halo, CF3, CN, etc.; n = 0-3; R3 = halo, CF3, CN, etc.], useful as an anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of the quinoline II was given. The compds. I tested had IC50's < 0.5 μM in assay to detect MEK inhibition.

MSTR 1



G4 = 6

L5 ANSWER 2 OF 3 MARPAT COPYRIGHT 2006 ACS on STN (Continued)



G22 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G25)
G33 = 23

Patent location: claim 1
Note: or pharmaceutically acceptable salts
Note: additional derivatization also claimed
Note: substitution is restricted

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

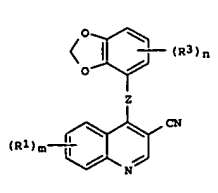
FORMAT

L5 ANSWER 3 OF 3 MARPAT COPYRIGHT 2006 ACS on STN

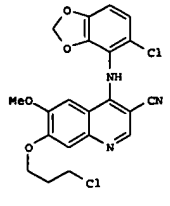
ACCESSION NUMBER: 138:137293 MARPAT
TITLE: Preparation of benzodioxolyl-substituted quinolines as tyrosine kinase inhibitors for treatment of solid tumors
INVENTOR(S): Hennequin, Laurent Francois Andre
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008409	A1	20030130	WO 2002-GB3177	20020710
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1409481	A1	20040421	EP 2002-745602	20020710
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2004536860	T2	20041209	JP 2003-513968	20020710
US 2005009867	A1	20050113	US 2004-483782	20040811
PRIORITY APPLN. INFO.:			EP 2001-401895	20010716
			EP 2001-403123	20011205
			WO 2002-GB3177	20020710

GI



I



II

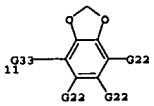
AB Title compds. I [wherein Z = O, S, SO, SO2, NR2, or C(R2)2; R2 = independently H or alkyl; m = 0-4; R1 = independently halo, CF3, CN, NC,

L5 ANSWER 3 OF 3 MARPAT COPYRIGHT 2006 ACS on STN (Continued)
NO2, OH, SH, NH2, CHO, CO2H, carbamoyl, alkyl, alkenyl, alkynyl, sulfamoyl, etc.; n = 0-3; R3 = halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, carbamoyl, alkyl, alkenyl, alkynyl, sulfamoyl, etc.; and pharmaceutically acceptable salts thereof) were prepd. for use anti-invasive agents in the containment and/or treatment of solid tumor disease. For example, 6-chloro-2,3-methylenedioxyaniline was coupled with 4-chloro-7-(3-chloropropoxy)-3-cyano-6-methoxyquinoline (prepn. of starting materials given) to give II. Test compds. inhibited the phosphorylation of a tyrosine contg. polypeptide substrate by c-Src kinase and the proliferation of c-Src transfected mouse NIH 3T3 fibroblast cells with IC50 values in the range of 0.001 μM to 10 μM and 0.01 μM to 20 μM, resp. In addn., I inhibited the migration of human A549 tumor cells and the growth of A549 xenograft tumors in athymic nude mice with activities in the range of 0.1 μM to 25 μM and 1-200 mg/kg/day, resp.

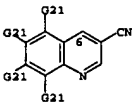
MSTR 1

G4—G1

G1 = 11



G4 = 6



G22 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G25)
G33 = 23

L5 ANSWER 3 OF 3 MARPAT COPYRIGHT 2006 ACS on STN (Continued)

Patent location: claim 1
Note: or pharmaceutically acceptable salts
Note: additional derivatization also claimed
Note: substitution is restricted
Note: also incorporates claim 8

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

10/520,468

```
=> d his

     (FILE 'HOME' ENTERED AT 14:11:39 ON 08 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 14:11:52 ON 08 MAR 2006
L1              STRUCTURE UPLOADED
L2            8 S L1 SAM
L3           69 S L1 FULL

     FILE 'CA' ENTERED AT 14:12:18 ON 08 MAR 2006
L4            3 S L3

     FILE 'MARPAT' ENTERED AT 14:12:42 ON 08 MAR 2006
L5            3 S L1 FULL

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:13:38 ON 08 MAR 2006
```